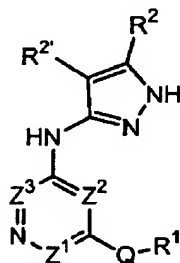


Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 1 (Currently amended): A compound of formula III:



III

or a pharmaceutically acceptable derivative or prodrug thereof, wherein:

Z^1 is nitrogen or CR^8 , Z^2 is ~~nitrogen or~~ CH, and Z^3 is nitrogen or CR^x , provided that when one of

Z^1 ~~and or~~ Z^3 is nitrogen, the other of Z^1 or Z^3 is CR^8 or CR^x , respectively;

R^x is T- R^3 or L-Z- R^3 ;

Q is selected from -N(R^4)-, -O-, -S-, or -CH(R^6)-;

R^1 is T-(Ring D);

Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl, said heteroaryl or heterocyclyl ring having 1-4 ring heteroatoms selected from nitrogen, oxygen or sulfur, wherein each substitutable ring carbon of Ring D is independently substituted by oxo, T- R^5 , or V-Z- R^5 , and each substitutable ring nitrogen of Ring D is independently substituted by - R^4 ;

T is a valence bond or a C_{1-4} alkylidene chain, wherein when Q is -CH(R^6)-, a methylene unit of said C_{1-4} alkylidene chain is optionally replaced by -O-, -S-, -N(R^4)-, -CO-, -OC(O)NH-, or -NHCO₂-;

Z is a C_{1-4} alkylidene chain;

L is -O-, -S-, -SO-, -SO₂-, -N(R^6)SO₂-, -SO₂N(R^6)-, -N(R^6)-, -CO-, -CO₂-, -N(R^6)CO-, -N(R^6)C(O)O-, -N(R^6)CON(R^6)-, -N(R^6)SO₂N(R^6)-, -N(R^6)N(R^6)-, -C(O)N(R^6)-, -OC(O)N(R^6)-, -C(R^6)₂O-, -C(R^6)₂S-, -C(R^6)₂SO-, -C(R^6)₂SO₂-, -C(R^6)₂SO₂N(R^6)-,

$-C(R^6)_2N(R^6)-$, $-C(R^6)_2N(R^6)C(O)-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$,
 $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, or $-C(R^6)_2N(R^6)CON(R^6)-$;

R^2 and $R^{2'}$ are independently selected from $-R$, $-T-W-R^6$, or R^2 and $R^{2'}$ are taken together with their intervening atoms to form a fused, 5-8 membered, unsaturated or partially unsaturated, ring having 0-3 ring heteroatoms selected from nitrogen, oxygen, or sulfur, wherein each substitutable ring carbon of said fused ring formed by R^2 and $R^{2'}$ is independently substituted by halo, oxo, $-CN$, $-NO_2$, $-R^7$, or $-V-R^6$, and each substitutable ring nitrogen of said ring formed by R^2 and $R^{2'}$ is independently substituted by R^4 ;

R^3 is selected from $-R$, $-halo$, $-OR$, $-C(=O)R$, $-CO_2R$, $-COCOR$, $-COCH_2COR$, $-NO_2$, $-CN$,
 $-S(O)R$, $-S(O)_2R$, $-SR$, $-N(R^4)_2$, $-CON(R^7)_2$, $-SO_2N(R^7)_2$, $-OC(=O)R$, $-N(R^7)COR$,
 $-N(R^7)CO_2(C_{1-6} \text{ aliphatic})$, $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, $-C=N-OR$, $-N(R^7)CON(R^7)_2$,
 $-N(R^7)SO_2N(R^7)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^7)_2$;

each R is independently selected from hydrogen or an optionally substituted group selected from C_{1-6} aliphatic, C_{6-10} aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms;

each R^4 is independently selected from $-R^7$, $-COR^7$, $-CO_2$ (optionally substituted C_{1-6} aliphatic),
 $-CON(R^7)_2$, or $-SO_2R^7$;

each R^5 is independently selected from $-R$, $halo$, $-OR$, $-C(=O)R$, $-CO_2R$, $-COCOR$, $-NO_2$, $-CN$,
 $-S(O)R$, $-SO_2R$, $-SR$, $-N(R^4)_2$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, $-OC(=O)R$, $-N(R^4)COR$,
 $-N(R^4)CO_2$ (optionally substituted C_{1-6} aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, $-C=N-OR$,
 $-N(R^4)CON(R^4)_2$, $-N(R^4)SO_2N(R^4)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^4)_2$;

V is $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-N(R^6)SO_2-$, $-SO_2N(R^6)-$, $-N(R^6)-$, $-CO-$, $-CO_2-$, $-N(R^6)CO-$,
 $-N(R^6)C(O)O-$, $-N(R^6)CON(R^6)-$, $-N(R^6)SO_2N(R^6)-$, $-N(R^6)N(R^6)-$, $-C(O)N(R^6)-$,
 $-OC(O)N(R^6)-$, $-C(R^6)_2O-$, $-C(R^6)_2S-$, $-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$,
 $-C(R^6)_2N(R^6)-$, $-C(R^6)_2N(R^6)C(O)-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$,
 $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, or $-C(R^6)_2N(R^6)CON(R^6)-$;

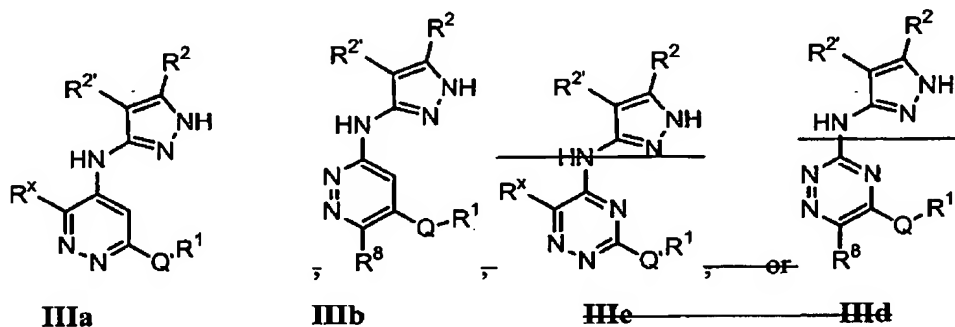
W is $-C(R^6)_2O-$, $-C(R^6)_2S-$, $-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$, $-C(R^6)_2N(R^6)-$, $-CO-$,
 $-CO_2-$, $-C(R^6)OC(O)-$, $-C(R^6)OC(O)N(R^6)-$, $-C(R^6)_2N(R^6)CO-$, $-C(R^6)_2N(R^6)C(O)O-$,
 $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$, $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$,
 $-C(R^6)_2N(R^6)CON(R^6)-$, or $-CON(R^6)-$;

each R^6 is independently selected from hydrogen or an optionally substituted C_{1-4} aliphatic group, or two R^6 groups on the same nitrogen atom are taken together with the nitrogen atom to form a 5-6 membered heterocyclyl or heteroaryl ring;

each R^7 is independently selected from hydrogen or an optionally substituted C_{1-6} aliphatic group, or two R^7 on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl or heteroaryl ring; and

R^8 is selected from -R, halo, -OR, -C(=O)R, -CO₂R, -COCOR, -NO₂, -CN, -S(O)R, -SO₂R, -SR, -N(R⁴)₂, -CON(R⁴)₂, -SO₂N(R⁴)₂, -OC(=O)R, -N(R⁴)COR, -N(R⁴)CO₂(optionally substituted C_{1-6} aliphatic), -N(R⁴)N(R⁴)₂, -C=NN(R⁴)₂, -C=N-OR, -N(R⁴)CON(R⁴)₂, -N(R⁴)SO₂N(R⁴)₂, -N(R⁴)SO₂R, or -OC(=O)N(R⁴)₂.

Claim 2 (Currently amended): The compound according to claim 1, wherein Q is -N(R⁴)-, -S-, or -CH(R⁶)-, and said compound is of formula **IIIa**, **IIIb**, **IIIc**, or **IIId**:



or a pharmaceutically acceptable derivative or prodrug thereof.

Claim 3 (Original): The compound according to claim 2, wherein said compound has one or more features selected from the group consisting of:

- (a) R^x is hydrogen, alkyl- or dialkylamino, acetamido, or a C_{1-4} aliphatic group;
- (b) R^1 is T-(Ring D), wherein T is a valence bond or a methylene unit;
- (c) Ring D is a 5-7 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and
- (d) R^2 is -R or -T-W- R^6 and $R^{2'}$ is hydrogen, or R^2 and $R^{2'}$ are taken together to form an optionally substituted benzo ring.

Claim 4 (Original): The compound according to claim 3, wherein:

- (a) R^x is hydrogen, alkyl- or dialkylamino, acetamido, or a C_{1-4} aliphatic group;
- (b) R^1 is T-(Ring D), wherein T is a valence bond or a methylene unit;
- (c) Ring D is a 5-7 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and
- (d) R^2 is -R or -T-W- R^6 and $R^{2'}$ is hydrogen, or R^2 and $R^{2'}$ are taken together to form an optionally substituted benzo ring.

Claim 5 (Original): The compound according to claim 3, wherein said compound has one or more features selected from the group consisting of:

- (a) R^1 is T-(Ring D), wherein T is a valence bond, and Q is -S- or -NH-;
- (b) Ring D is a 5-6 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and
- (c) R^2 is -R and $R^{2'}$ is hydrogen, wherein R is selected from hydrogen, C_{1-6} aliphatic, phenyl, a 5-6 membered heteroaryl ring, or a 5-6 membered heterocyclic ring.

Claim 6 (Original): The compound according to claim 5, wherein:

- (a) R^1 is T-(Ring D), wherein T is a valence bond, and Q is -S- or -NH-;
- (b) Ring D is a 5-6 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and
- (c) R^2 is -R and $R^{2'}$ is hydrogen, wherein R is selected from hydrogen, C_{1-6} aliphatic, phenyl, a 5-6 membered heteroaryl ring, or a 5-6 membered heterocyclic ring.

Claim 7 (Original): The compound according to claim 5, wherein said compound has one or more features selected from the group consisting of:

- (a) R^x is hydrogen methyl, ethyl, propyl, cyclopropyl, isopropyl, methylamino or acetamido;
- (b) R^1 is T-(Ring D), wherein T is a valence bond and Ring D is a 5-6 membered aryl or heteroaryl ring, wherein Ring D is optionally substituted with one to two groups selected from -halo, -CN, -NO₂, -N(R^4)₂, optionally substituted C_{1-6} aliphatic group,

-OR, -CO₂R, -CON(R⁴)₂, -OCO(R⁴)₂, -N(R⁴)COR, -N(R⁴)SO₂R,
 -N(R⁶)COCH₂CH₂N(R⁴)₂, or -N(R⁶)COCH₂CH₂CH₂N(R⁴)₂; and

(c) R² is hydrogen or a substituted or unsubstituted C₁₋₆ aliphatic.

Claim 8 (Original): The compound according to claim 7, wherein:

- (a) R^x is hydrogen methyl, ethyl, propyl, cyclopropyl, isopropyl, methylamino or acetamido;
- (b) R¹ is T-(Ring D), wherein T is a valence bond and Ring D is a 5-6 membered aryl or heteroaryl ring, wherein Ring D is optionally substituted with one to two groups selected from -halo, -CN, -NO₂, -N(R⁴)₂, optionally substituted C₁₋₆ aliphatic group, -OR, -CO₂R, -CON(R⁴)₂, -OCO(R⁴)₂, -N(R⁴)COR, -N(R⁴)SO₂R, -N(R⁶)COCH₂CH₂N(R⁴)₂, or -N(R⁶)COCH₂CH₂CH₂N(R⁴)₂; and
- (c) R² is hydrogen or a substituted or unsubstituted C₁₋₆ aliphatic.

Claim 9 (Currently amended): A compound selected from the group consisting of:

~~N⁵-(1H-Indazol-6-yl)-N³-(5-methyl-1H-pyrazol-3-yl)-[1,2,4]triazine-3,5-diamine;~~
~~N-[4-[3-(5-Methyl-1H-pyrazol-3-ylamino)-[1,2,4]triazin-5-ylsulfanyl]-phenyl]-acetamide;~~
~~[5-(3-Methoxy-benzyl)-[1,2,4]triazin-3-yl]-(5-methyl-1H-pyrazol-3-yl)-amine;~~
~~N³-(5-Cyclopropyl-1H-pyrazol-3-yl)-N⁵-pyridin-3-ylmethyl-[1,2,4]triazine-3,5-diamine;~~
~~[5-(Benzothiazol-6-ylsulfanyl)-[1,2,4]triazin-3-yl]-(5-cyclopropyl-1H-pyrazol-3-yl)-amine;~~
~~[4-[3-(5-Cyclopropyl-1H-pyrazol-3-ylamino)-[1,2,4]triazin-5-yloxy]-phenyl]-acetonitrile;~~
~~N-[4-[3-(1H-Indazol-3-ylamino)-[1,2,4]triazin-5-ylamino]-phenyl]-methanesulfonamide;~~
~~(1H-Indazol-3-yl)-[5-(thiophen-2-ylmethylsulfanyl)-[1,2,4]triazin-3-yl]-amine;~~
~~N⁵-(5-Methyl-1H-pyrazol-3-yl)-N³-pyridin-3-ylmethyl-[1,2,4]triazine-3,5-diamine;~~
~~[3-(Benzothiazol-6-ylsulfanyl)-[1,2,4]triazin-5-yl]-(5-methyl-1H-pyrazol-3-yl)-amine;~~
~~[4-[5-(5-Methyl-1H-pyrazol-3-ylamino)-[1,2,4]triazin-3-yloxy]-phenyl]-acetonitrile;~~
~~N⁵-(5-Cyclopropyl-1H-pyrazol-3-yl)-N³-(1H-indazol-6-yl)-[1,2,4]triazine-3,5-diamine;~~
~~N-[4-[5-(5-Cyclopropyl-1H-pyrazol-3-ylamino)-[1,2,4]triazin-3-ylsulfanyl]-phenyl]-acetamide;~~
~~N⁵-(1H-Indazol-3-yl)-N³-(1H-indazol-6-yl)-[1,2,4]triazine-3,5-diamine;~~
~~(1H-Indazol-3-yl)-[3-(3-methoxy-phenylsulfanyl)-[1,2,4]triazin-5-yl]-amine;~~
~~N⁵-(1H-Indazol-6-yl)-N³-(5-methyl-1H-pyrazol-3-yl)-pyridazine-3,5-diamine;~~

N-{4-[6-(5-Methyl-1*H*-pyrazol-3-ylamino)-pyridazin-4-ylsulfanyl]-phenyl}-acetamide;
[5-(3-Methoxy-benzyl)-pyridazin-3-yl]-(5-methyl-1*H*-pyrazol-3-yl)-amine;
N³-(5-Cyclopropyl-1*H*-pyrazol-3-yl)-N⁵-pyridin-3-ylmethyl-pyridazine-3,5-diamine;
[5-(Benzothiazol-6-ylsulfanyl)-pyridazin-3-yl]-(5-cyclopropyl-1*H*-pyrazol-3-yl)-amine;
{4-[6-(5-Cyclopropyl-1*H*-pyrazol-3-ylamino)-pyridazin-4-yloxy]-phenyl}-acetonitrile;
N-{4-[6-(1*H*-Indazol-3-ylamino)-pyridazin-4-ylamino]-phenyl}-methanesulfonamide;
(1*H*-Indazol-3-yl)-[5-(thiophen-2-ylmethylsulfanyl)-pyridazin-3-yl]-amine;
N⁵-(5-Methyl-1*H*-pyrazol-3-yl)-N³-pyridin-3-ylmethyl-pyridazine-3,5-diamine;
[6-(Benzothiazol-6-ylsulfanyl)-pyridazin-4-yl]-(5-methyl-1*H*-pyrazol-3-yl)-amine;
{4-[5-(5-Methyl-1*H*-pyrazol-3-ylamino)-pyridazin-3-yloxy]-phenyl}-acetonitrile;
N⁵-(5-Cyclopropyl-1*H*-pyrazol-3-yl)-N³-(1*H*-indazol-6-yl)-pyridazine-3,5-diamine;
N-{4-[5-(5-Cyclopropyl-1*H*-pyrazol-3-ylamino)-pyridazin-3-ylsulfanyl]-phenyl}-acetamide;
N⁵-(1*H*-Indazol-3-yl)-N³-(1*H*-indazol-6-yl)-pyridazine-3,5-diamine; and
(1*H*-Indazol-3-yl)-[6-(3-methoxy-phenylsulfanyl)-pyridazin-4-yl]-amine.

Claim 10 (Original): A composition comprising a compound according to any of claims 1-9, and a pharmaceutically acceptable carrier.

Claim 11 (Original): The composition according to claim 10, further comprising an additional therapeutic agent.

Claim 12 (Original): A method of inhibiting Aurora-2 or GSK-3 activity in a biological sample comprising the step of contacting said biological sample with a compound according to any one of claims 1-9.

Claim 13 (Original): A method of inhibiting Aurora-2 activity in a patient comprising the step of administering to said patient a composition according to claim 10.

Claim 14 (Original): A method of inhibiting Aurora-2 activity in a patient comprising the step of administering to said patient a composition according to claim 11.

Claim 15 (Original): A method of treating an Aurora-2-mediated disease, which method

comprises administering to a patient in need of such a treatment a therapeutically effective amount of a composition according to claim 10.

Claim 16 (Original): The method according to claim 15, wherein said disease is selected from colon, breast, stomach, or ovarian cancer.

Claim 17 (Original): The method according to claim 16, wherein said method further comprises administering an additional therapeutic agent.

Claim 18 (Original): The method according to claim 17, wherein said additional therapeutic agent is a chemotherapeutic agent.

Claim 19 (Original): A method of inhibiting GSK-3 activity in a patient comprising the step of administering to said patient a composition according to claim 10.

Claim 20 (Original): A method of inhibiting GSK-3 activity in a patient comprising the step of administering to said patient a composition according to claim 11.

Claim 21 (Original): A method of method of treating a GSK-3-mediated disease, which method comprises administering to a patient in need of such a treatment a therapeutically effective amount of a composition according to claim 10.

Claim 22 (Original): The method according to claim 21, wherein said GSK-3-mediated disease is selected from diabetes, Alzheimer's disease, Huntington's Disease, Parkinson's Disease, AIDS-associated dementia, amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), schizophrenia, cardiomyocyte hypertrophy, reperfusion/ischemia, or baldness.

Claim 23 (Original): The method according to claim 22, wherein said GSK-3-mediated disease is diabetes.

Claim 24 (Original): A method of enhancing glycogen synthesis or lowering blood levels of glucose in a patient in need thereof, which method comprises administering to said patient a therapeutically effective amount of a composition according to claim 10.

Claim 25 (Original): A method of inhibiting the production of hyperphosphorylated Tau protein in a patient, which method comprises administering to a patient in need thereof a therapeutically effective amount of a composition according to claim 10.

Claim 26 (Original): A method of inhibiting the phosphorylation of β -catenin, which method comprises administering to a patient in need thereof a therapeutically effective amount of a composition according to claim 10.

Applicants request entry of the above amendments, favorable consideration of the application, and early allowance of the pending claims.

Respectfully submitted,

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